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Chemistry

Cummings
~~Quick~~
~~Patterson~~
File 3E1364

AUG 9 1973

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

BRIEFING MEMORANDUM
Crown Zellerbach Corp.
Camas, Washington 98607

Pesticide Petition No. 3E1364--
Establishment of Exemption from
Tolerance for Dimethyl Sulfoxide

DEPUTY ASSISTANT ADMINISTRATOR
FOR PESTICIDE PROGRAMS

1. A proposal was published in the Federal Register of June 22, 1973 (38 F.R. 16392), proposing establishment of an exemption from the requirement of a tolerance (§ 180.1001(d)) for residues of dimethyl sulfoxide when used as a solvent or cosolvent in pesticide formulations intended for preemergence application or application prior to formation of edible parts of food plants. Copies of the proposal and briefing memorandum that accompanied it are attached. No comments or requests for referral to an advisory committee were received.

2. We recommend that the attached order be signed and published.

Edward Gross, Editor
Federal Register Documents

APPROVED:

Lee E. TerBush, Acting Chief Coordination Branch	John B. Ritch, Jr., Acting Director Registration Division

cc: Branch file; DMBaker; P.Critchlow; EEB; Chemistry Branch; Toxicology Br.;
EGross EG:el 8/1/73; RDInit. PChichilo 7/28/73

AUG 9 1973

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CB

JUN 12 1973

BRIEFING MEMORANDUM
Crown Zellerbach Corp.
Camas, WA 98607

Pesticide Petition No. 3E1364
Dimethyl Sulfoxide Proposed Exemption—Amend § 180.1001(d)

DEPUTY ASSISTANT ADMINISTRATOR
FOR PESTICIDE PROGRAMS

1. Dimethyl sulfoxide is presently exempted from the requirement of a tolerance (§ 180.1001(d)) as a solvent for pesticide formulations used before crop emerges from soil; i.e., preemergence use only. Crown Zellerbach submitted this petition proposing establishment of an exemption from the requirement of a tolerance for residues of dimethyl sulfoxide in or on raw agricultural commodities when used as an inert solvent or cosolvent in pesticide formulations applied preemergence to growing crops or prior to formation of edible parts of food plants.

2. Dimethyl sulfoxide has been found useful for the purpose for which an exemption from the requirement of a tolerance is sought.

3. The Chemistry Branch concludes that combined residues of dimethyl sulfoxide and its sulfone resulting from the proposed use, as limited, will not exceed 1 ppm in crops.

4. The Toxicology Branch finds the proposed exemption safe and that it will protect the public health.

5. We recommend that the attached proposal be signed and published.

Edward Gross, Editor
Federal Register Documents

APPROVED:

JUN 18 1973

Lee E. TerBush
Acting Chief
Coordination Branch

John B. Ritch, Jr.
Acting Director
Registration Division

cc: Div. file
Branch file, CB, TB, Ms Critchlow, EEB, Mr. Ramsey/FDA, Mr. Gross

EGross:ggr:6/1/73
R/D Init:CHWilliams:5/31/73
PChichilo:5/31/73

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CERTIFIED

Chem. Br

Registration Division

Opinion on Usefulness
Pesticide Petition 3E1364

Lee E. TerBush
Acting Chief
Coordination Branch

Pesticide Petition 3E1364 proposing an exemption from the requirement of a tolerance for the solvent dimethyl sulfoxide when used in pesticide formulations applied preemergence or applied prior to formation of edible parts of food plants was submitted by the Crown Zellerbach Company.

After examining this petition, it is the opinion of the Chemistry Branch that the pesticide chemical is useful for the purpose for which an exemption from the requirement of a tolerance is sought.

P. C. Critchlow
Acting Head,
Registration Section
Coordination Branch

Woodward

File: PP # 3E1364

EPA:RD:SX:PCCritchlow:LMS: 5/22/73
cc: Coor. Br.
CB
TB
EEB

MAY 29 1973

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ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Date: April 27, 1973

Reply to Attn of:

Subject: DMSO - Exempted product.

To: Mr. Lee E. TerBush, Acting Chief
Coordination Branch
Registration Division

Pesticide Petition No. 3E1364

Crown Zellerbach Corp.
Camas, Washington 98607

The petitioner wishes to change the present exemption for dimethyl sulfoxide [Sec. 180.1001(d)] to the following:

Limits: For use in preemergence application and application prior to formation of edible parts of food plants.

Use: Solvent, cosolvent.

In the memo by Mr. Andrew R. Rathman 4/18/73 he defers to the Toxicology Branch with the following statement; "If TB needs information on the actual residue levels expected in meat, milk, poultry, and eggs, appropriate feeding studies will be needed." He also states in his conclusions that, "even though available data do not reflect the maximum application rate we might expect to occur we conclude that the combined residues of DMSO and $DMSO_2$ would not exceed 1 ppm".

Conclusions

TB finds this amendment will not alter our previous recommendation of establishing an exemption from a tolerance for DMSO.

Robert P. Schmidt 4/27/73

Robert P. Schmidt, D.V.M.
Toxicology Branch/RD

cc: Chemistry Branch
Ecological Effects Branch
Division Reading File
Branch Reading File
PP# 3E1364

APR 30 1973

R/D Init:CHWilliams 4/27/73
RPSchmitd:dtb 4/27/73
Init:CHWilliams

4/27/73

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File: PP# 3E1364

April 18, 1973

PP #3E1364. Comments on proposed revision of the present DMSO exemption.

Coordination Branch
and Toxicology Branch, RD

Crown Zellerbach Corporation proposes that the present exemption for dimethyl sulfoxide [Section 180.1001(d)] be amended to the following:

> Use: For use in preemergence application and application prior to formation of edible parts of food plants.
>
> Limits: Solvent, cosolvent.*

The present exemption limits the use to a maximum dose of 1 lb/acre in pesticide formulations intended for use for corn and soybeans before crop emerges from the soil.

In order to liberalize the present DMSO exemption, the petitioner has now submitted additional data reflecting application of DMSO to many different crops.

The study reflects application of ^{35}S DMSO to 27 crops at a rate equivalent to one lb/A and to six crops at a rate equivalent to 5 lbs/A. The crops treated at the one lb rate reflect commodities from 13 different crop groupings. The crops treated at the 5 lb rate include corn, rice, potatoes, soybeans, peanuts, and cotton. All crops were field grown with the exception of rice which was grown in a greenhouse. In all cases, the crops received a single post-emergence application at the time when the first sign of edible plant formation was noted.

All analyses were performed by a very slightly modified version of the radiotracer technique utilized to determine residues in connection with PP #1E1017 (see W. J. Boodee review dated 8/28/71).

In our review of PP #1F1026 (proposed exemption for dimethyl formamide) dated 12/21/70, we estimated the maximum application rate of DMF would be 6 lbs/A. We believe this rate would also be a reasonable maximum in the use of DMSO. Therefore, the petitioner's data reflect ca. 1/6 and 5/6X our calculated maximum rate.

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*Apparently, the petitioner inadvertently reversed the "use" and "limits" in his proposal. Any final regulation should list the use as a solvent, cosolvent and the limits as preemergenee application, etc.

At the one lb application rate, total activity calculated as DMSO ranged from <0.01-0.37 ppm. Generally, at least one crop from each group was further subjected to TLC analysis to determine residues of DMSO and $DMSO_2$ (the sulfone). Combined DMSO and $DMSO_2$ residues (from the 1 lb rate) ranged from <0.01-0.06 ppm.

At the 5 lb application rate, total residues calculated as DMSO ranged from 0.34-2.47 ppm. At the 5 lb rate, all samples were subjected to analyses for DMSO and $DMSO_2$. Combined DMSO and $DMSO_2$ residues ranged from 0.03-0.27 ppm.

Even though the available data do not reflect the maximum application rate we might expect to occur, we conclude that combined residues of DMSO and $DMSO_2$ would not exceed 1 ppm.

No conventional large animal feeding studies are available from the feeding of DMSO. Several radiotracer studies are available reflecting oral intake of DMSO in small animals (rabbits and dogs). The studies indicate that a maximum of ca. 10% of the activity could be stored in animals (a more precise figure is not possible since no complete balance study is available). The Company has calculated residue levels of DMSO in meat, milk, poultry, and eggs based upon the assumption that 10% of the DMSO intake will accumulate entirely in the commodity of interest and that all the feed will contain residues of DMSO at 0.16 ppm (the highest DMSO residue detected in any crop of this petition). From these assumptions, the Company calculates that residues in eggs would be 0.05 ppm, 0.03 ppm in poultry, 0.27 ppm in beef tissues, and 0.05 ppm in milk. If we take the maximum DMSO plus $DMSO_2$ residue (which was 0.27 ppm) and use the petitioner's rationale, residues in the various tissues would range from 0.05-0.45 ppm. We defer to TB as to their concern over these theoretical levels possible in meat, milk, poultry, and eggs (TB should realize that these levels are only calculated maxima and we emphasize that these studies do not reflect feeding of DMSO to livestock.) If TB should need data on actual residue levels expected in meat, milk, poultry and eggs, then appropriate feeding studies will be needed.

Conclusions

1. From the use as limited, we would not expect combined residues of DMSO and $DMSO_2$ to exceed 1 ppm in crops.

2. On the basis of small animal studies, the petitioner has calculated residue levels to be expected in meat, milk, poultry, and eggs. These calculations are of little real value. We defer to TB as to their concern over residue levels expected in these commodities. If TB needs information on the actual residue levels expected in meat, milk, poultry, and eggs, appropriate feeding studies will be needed.

Recommendations

Pharmacological considerations permitting, we recommend for the proposed exemption.

Note to COB: Any final regulation should have the "Use" and "Limits" reversed from what the petitioner has proposed.

Andrew R. Rathman
Chemistry Branch
Registration Division

cc:
Tox.Br.
RO-130(FDA)
P.Critchlow
C.Lewis(Chamblee)
H.Enos(Perrine)
Ecol. Eff. Br.
Chem. Br.
Glasgow
PP #3F1364

ARRathman:jrf
4/18/73
RD/I - RSQuick-4/10/73
JGCummings-4/16/73

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Chem. W.

ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Date: March 28, 1973

Reply to Attn of:

Subject: DMSO - Amendment

To: Mr. Lee E. TerBush, Acting Chief
Coordination Branch
Registration Division

Pesticide Petition No. 3F1364

Crown Zellerbach Corp.
Camas, Washington 98607

On May 4, 1972 a conference was held with Mr. Chapman and Dr. Smale from Crown Zellerbach about the possibility of changing the limitations for the use of DSMO. The proposals are as follows:

The current limitations on dimethyl sulfoxide as set forth in 40 CFR 180.1001(d) are:

USE	:	Solvent for formulations used before crop emerges from soil.
LIMITS	:	Maximum dosage rate one (1) pound per acre. Used in pesticide formulations intended only for corn and soybeans.

Based on the data contained in this proposal we request that the above limitations be amended to:

USE	:	For use in preemergence application and application prior to formation of edible parts of food plants.
LIMITS	:	Solvent, cosolvent.

MAR 30 1973

In this meeting Mr. G. Beusch was concerned about the possible residues in food products. It was suggested that a complete radioactive tracer study be done on apples, lettuce, peppers and onions. Data submitted at this time are to satisfy Chemistry's request. These data indicate that at 5x the proposed application rate residues still fall within the recommended safety level. Although no actual ruminant feeding study was completed calculated residue levels for meat, milk and eggs were submitted; calculations were based upon radioactive tracer studies on rats, rabbits, beagles and man.

The Toxicology Branch finds that the data submitted with this amendment does not alter our previous findings of 12/16/71 and recommends that DMSO be exempted from a tolerance.

Robert P. Schmidt 3/28/73

Robert P. Schmidt, D.V.M.
Toxicology Branch
Registration Division

cc: Chemistry Branch
Ecological Effects Branch
Division Reading File
Branch Reading File
PP# 3F1364

R/D Init:CHWilliams 3/28/73
RPSchmidt:dtb 3/28/73
Init:CHWilliams

CHW 3/28/73

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Chem. Br.

[illegible]

March 14, 1973

Pesticide Petition No. ~~1E1017~~ 3E1364

4/30/73

~~Coordinator~~
~~Woodward~~
~~Gooch~~

File PP# 3E1364

Mr. J. A. Chapman, General Manager
Chemical Products Division
Crown Zellerbach Corporation
Camas, Washington 98607

Dear Mr. Chapman:

This acknowledges your letter of February 23, 1973, transmitting a certified check for $2,000; and a request that Pesticide Petition No. 1E1017 be amended to propose a revision in the use and limits of dimethyl sulfoxide in § 180.1001(d).

Pesticide Petition No. 1E1017 has been regulated, therefore, your submittal is being considered as a new petition under § 408(a) of the Federal Food, Drug and Cosmetic Act. We note you are proposing that § 180.1001(d) be amended for dimethyl sulfoxide as follows:

USE: For use in preemergence application and application prior to formation of edible parts of food plants.

LIMITS: Solvent, cosolvent.

The request has been designated Pesticide Petition No. 3E1364. Further action awaits completion of scientific review and evaluation.

Sincerely yours,

Hamilton K. Parran, Jr.
Petitions Control Officer
Coordination Branch

cc: Division file
Branch file, Fiscal Branch, CB, TB, EEB, Mrs. Critchlow

HMParran:ggr:3/16/73
R/D Init:PChichilo:3/14/73
LETerBush:3/14/73

MAR 21 1973

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Chemical:	**Dimethyl sulfoxide**
PC Code:	**900177**
HED File Code	**11500 Petition Files Chemistry**
Memo Date:	**03/09/2004**
File ID:	**00000000**
Accession Number:	***412-05-4000***

HED Records Reference Center
09/08/2004